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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/560,803	04/28/2000	Won-Bin Young	P04014US1	5114

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SUITE 3200  
DES MOINES, IA 50309-2721

EXAMINER

WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 05/06/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/560,803

Applicant(s)

YOUNG ET AL.

Examiner

Ulrike Winkler, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 February 2002.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 11-13, 15-25, 34 and 36-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10, 14, 26-33, 35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

The Amendment filed February 15, 2002 (Paper No. 9) in response to the Office Action of October 1, 2001 is acknowledged and has been entered. Claims 1-10, 14, 25-3 and 35 are currently being examined. Applicant noted on page 4 of the response that claims 11-13, 15-25, 34 and 36-39 are to be canceled, yet applicant provided no formal instructions for doing so, correction is requested.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The Office acknowledges the deletion of the embedded hyperlink from the specification.

The Office acknowledges applicant's attempt to correct the drawings, but upon review by the draftsman the new drawings were found to contain minor informalities. Please see notice of Draftsman's Review. Correction is required.

The objection of claim 35 is withdrawn in view of applicant's amendment.

The rejection of claims 1-10, 14, 26-33 and 35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **maintained**. The term "increasing" is indefinite because the ordinary artisan would not know how to determine the requisite quantity necessary to be considered "increasing" and what this value is compared to. The amended claim now reads

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“sufficiently increasing” which does not help clarify the claim. It remains unclear how much viral titer production is required to be considered sufficiently increasing.

The rejection of the term “helper virus” **is withdrawn**; the definition of “helper virus” is interpreted to be (specification page 8 lines 14-30):

A plasmid that enables positive selection of cells with active helper virus. More particularly an internal ribosome entry site along with a marker selection gene downstream of the *gag*, *pol*, and *env* genes provided positive selection of helper virus which had not been inactivated by methylation. “Helper virus” shall include any packaging deficient vector or nucleotide sequence encoding a viral protein, the expression of which is necessary in a vector producing cell for assembly and packaging of a particular vector capsid.

The rejection of the term “viral vector” **is withdrawn**; the definition of “viral vector” is interpreted to be (specification page 9 lines 18-31):

Viral vector shall include any viral based vector which embodies less than all structural proteins necessary for viral capsid assembly, and any additional nucleotide sequences desirable for expression or to be delivered to; a host cell.

The rejection of claims 1, 6-10, 14, 26 and 27 under 35 U.S.C. 102(a) as being anticipated by Gram et al. (Journal of Hematotherapy, 1998) **is withdrawn**. The newly amended claim 1, requires the use of a helper virus that does not contain a packaging signal, will presumably integrate into the cell genome, contains the viral structural proteins and an internal ribosomal entry site that is linked to a selection marker. While Gram et al. teaches a vector construct that contains a packaging signal as well as selectable marker, it does not contain viral structural proteins.

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The rejection of claims 1-10, 14 26-33 and 35 under 35 U.S.C. 103(a) as being unpatentable over Miller (U.S. Pat. No. 5,766,945) and Gurtu et al. (BBRC 1996) in view of Gram et al. (J. of Hematotherapy 1998) **is withdrawn**.

New rejections necessitated by applicants amendments:

Claims 1, 2, 9, 26, 27 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All claims are referring to “inhibiting the presence of DNA methylation”, inhibiting implies the stopping of a metabolic process. Usually this is accomplished by the introduction of a compound that has an inhibitory effect. For example, 5-AZA-C is such a compound which has been shown to inhibit DNA methylation. In this case the “inhibiting the presence of DNA methylation” is actually referring to the selection of those cells in which the “helper virus” is not inserted into a region of the genome that is hypermethylated, thereby allowing for better transcription of the “helper virus” genes. This is not the same as actively interfering with the methylation process by the addition of an inhibitor. Therefore, selection of clones that are not methylated does not equate to inhibiting methylation.

In claims 1, 9, 10 and 14, it is not clear if Markush claim format was intended in claims 10 and 14. If a Markush format was intended the claim needs to have the following format “...are selected from a group consisting of A, B, C and D”. In order to be a proper Markush group the compounds included in a Markush group must (1) share a common utility and (2) share a substantial structural feature disclosed as being

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essential to that utility. The claims suggest a selection from a group, however, the claims provide a single option indicating that there can be no selection.

Claim 1 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There are several components which are not clear in the base claim to list a few:

a) it is not clear what applicant intends by “sufficiently increasing”, this implies that the method must be compared to another method yet the claim provides no insight as to which methods are compared in order to make a qualitative assessment that something is “sufficiently increased”.

b) “genome sequence viral structural proteins” is applicant referring to the helper virus comprising viral structural proteins?

c) “and a nucleotide sequence” it is not clear what nucleotide sequence is being referred to. Is this “nucleotide sequence” a gene of interest to be expressed in the host cell, or does “nucleotide sequence” refer to specific structures that have an effect on nucleotide sequences present in trans.

d) “capable of expressing an introduced viral components”, first of all on the grammatical aspect: “expressing an introduced” is singular while “viral components” is plural. Are these viral components referring to the “genome sequence viral structural proteins” found earlier in the claim? If not, there is insufficient antecedent basis for this term in the claim.

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The claim could be modified using the following suggestion. Applicant is advised that the following suggestion has not been checked for potential written description problems. It is applicant's responsibility to ensure that any amendments to the claims have proper support in the specification. The following claim suggestion merely illustrates what the Office understands the invention to be.

A method of producing viral particles:

- a) establishing a vector packaging cell line by introducing a helper virus construct into the cell, said helper virus encodes viral structural proteins and an internal ribosomal entry site linked to a selection marker,
- b) selecting for helper virus containing cells in which the helper virus DNA is not methylated by growing the cells in the presence of a selection agent,
- c) introducing a viral vector into the cells of step b, the viral vector comprises a viral packaging signal and a gene of interest, growing cells in the presence of the selection agent and collecting viral particles.

### ***Conclusion***

Claims 1-10, 14, 26-33 and 35 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

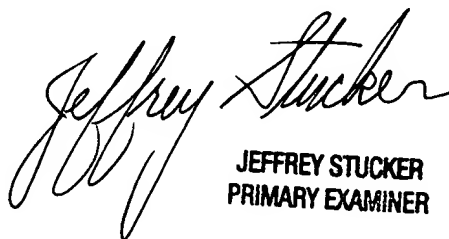
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 or for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Ulrike Winkler, Ph.D.

  
JEFFREY STUCKER  
PRIMARY EXAMINER